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CLINICAL INVESTIGATION

SEQUENTIAL COMPARISON OF SEED LOSS AND PROSTATE DOSIMETRY OF STRANDED SEEDS WITH LOOSE SEEDS IN ^{125}I PERMANENT IMPLANT FOR LOW-RISK PROSTATE CANCER

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Purpose: To compare stranded seeds (SSs) with loose seeds (LSs) in terms of prostate edema, dosimetry, and seed loss after ^{125}I brachytherapy.
Methods and Materials: Two prospective cohorts of 20 men participated in an institutional review board-approved protocols to study postimplant prostate edema and its effect on dosimetry. The LS cohort underwent brachytherapy between September 2002 and July 2003 and the SS cohort between April 2006 and January 2007. Both cohorts were evaluated sequentially using computed tomography-magnetic resonance imaging fusion-based dosimetry on Days 0, 7, and 30. No hormonal therapy or supplemental beam radiotherapy was used.
Results: Prostate edema was less in the SS cohort at all points (p = NS). On Day 0, all the prostate dosimetric factors were greater in the LS group than in the SS group ($p = 0.003$). However, by Days 7 and 30, the dosimetry was similar between the two cohorts. No seeds migrated to the lung in the SS cohort compared with a total of five seeds in 4 patients in the LS cohort. However, the overall seed loss was greater in the SS cohort (24 seeds in 6 patients; 1.1% of total vs. 0.6% for LSs), with most seeds lost through urine (22 seeds in 5 patients).
Conclusion: Despite elimination of venous seed migration, greater seed loss was observed with SSs compared with LSs, with the primary site of loss being the urinary tract. Modification of the technique might be necessary to minimize this. Prostate dosimetry on Days 7 and 30 was similar between the SS and LS cohorts. © 2008 Elsevier Inc.

Stranded seeds, Loose seeds, Seed loss, Prostate cancer, Permanent prostate brachytherapy.

INTRODUCTION

Permanent seed prostate brachytherapy using ^{125}I or ^{103}Pd seeds is an established treatment modality for favorable-risk prostate cancer. The migration of seeds to the lungs through the venous system is a concern with loose seeds (LSs) even though its effect on prostate dosimetry and normal tissue complications is unclear (1–7). Stranding technology (linking seeds in suture material or a polymer) has been shown to dramatically reduce seed migration to the lung (8–10).

The effect of stranding on prostate dosimetry is controversial (10–17). Seed migration and loss is not limited to the venous system but can also occur through other mechanisms (10, 18–20), such as through the urinary tract, ejaculation, or distal displacement due to the action of the perineal muscles. Loss through any of these mechanisms can have an effect on dosimetry, not only of the prostate, but also of the surrounding organs. Sequential evaluations in patients with permanent prostate brachytherapy are important to assess the changes in dosimetry resulting from the resolution of prostate edema, seed migration, seed movement or loss, and variations in the shape and position of critical organs such as the rectum (10, 11, 21–23).

A detailed sequential comparison of LSs and SSs with regard to seed loss, prostate edema, and dosimetry has not been previously reported. We have previously reported the results of a sequential evaluation of prostate edema using magnetic resonance imaging (MRI)-computed tomography (CT) fusion for postimplant dosimetry on Days 0, 7, and 30 in a prospective cohort of 20 men treated with ^{125}I LSs (22). We now report a similar evaluation of a cohort of 20 men treated with SSs, with the aim of studying strand stability and seed loss. Prostate edema and dosimetry were compared with the data from the previous LS cohort.

METHODS AND MATERIALS

The permanent seed prostate brachytherapy program at Princess Margaret Hospital/University Health Network began in March

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1999 and more than 1,000 patients have been treated. Between April 2006 and January 2007, 20 men with favorable-risk prostate cancer (prostate-specific antigen ≤10 ng/mL, Gleason score ≤6, and clinical Stage T1c-T2a) agreed at the time of brachytherapy mapping to an institutional review board-approved protocol to evaluate prostate edema and strand stability, as well as prostate and critical organ dosimetry. ^{125}I seeds were provided in preloaded 18-gauge needles, embedded in a polymer strand of glycolide, lactide, and polydiaxanone (supplied by BrachySciences, Oxford, CT). The strands were custom prepared according to the preplan and off-loaded centrally for urethral sparing (the four periurethral needles generally had one seed at the base and one at the apex, with no radioactivity centrally). All needles contained only SSs but terminated with a loose 5-mm spacer. The pretreatment variables, including prostate size (Table 1), were similar to the previous LS cohort (22). None of the patients had undergone previous hormonal therapy.

The pretreatment investigations, planning, implant procedure, postimplant dosimetry, and follow-up were performed according to our standard institutional approach (24), with the addition of CT-MRI scans on Days 0 and 7. Patients for whom the extra visit for the Day 7 scans did not require excessive travel were approached preferentially.

Prostate mapping was performed 2–4 weeks before brachytherapy using transrectal ultrasonography (TRUS) with a B and K Leopard (2001, B & K Medical, Wilmington, MA) at 6.5 MHz. Images were recorded every 5 mm and downloaded to the VariSeed, version 7.0, treatment planning system (Varian, Palo Alto, CA). The planning target volume was defined as the prostate with a 2–3-mm anterior and lateral margin and a 5-mm margin in the cranial and caudal directions. No posterior margin was added at the rectal interface. Preplan dosimetry aimed for a V_{100} >99% (percentage of the prostate volume receiving 100% of prescribed dose) and D_{90} of 120–125% (isodose enclosing 90% of the prostate volume (D_{90}) of 120–125%), and V_{150} of 55%, with the urethral dose limited to <125%. The seed activity for strands (median, 0.31 mCi; range, 0.29–0.32) was similar to that of the previous cohort treated with LSs (median, 0.31 mCi; range, 0.29-0.33). The prescribed dose was 145 Gy.

Table 1. Pretreatment variables

Variable	LSs	SSs
Age (y)		
Median	63	66
Range	52–74	44–77
Stage (%)		
T1c	70	60
T2a	30	40
Gleason score (%)		
6	100	95
5	0	5
PSA (ng/mL)		
Median	4.9	4.4
Range	2.4–8.7	2.3–10
Seeds (*n*)		
Median	108	109
Range	77–140	84–136
Activity/seed (mCi)		
Median	0.31	0.31
Range	0.29–0.32	0.29–0.33
Needles (*n*)		
Median	31	32
Range	23–43	26–39
Prostate volume (cm^3)		
Median	34.5	40.8
Range	15.9–57.3	23.9–60.2

Abbreviations: LSs = loose seeds; SSs = stranded seeds; PSA = prostate-specific antigen.

Implants were performed with the patients under general anesthesia and the needles inserted under TRUS and fluoroscopic guidance using a standard template. During both mapping and implantation, the urethra was identified with aerated gel. At the end of the procedure, a three-way Foley catheter was inserted for bladder irrigation and was removed after the Day 0 scans had been completed. Patients were discharged from the Short Stay Unit once they were able to pass urine satisfactorily.

Postimplant dosimetry, using CT-MRI fusion, was performed three times for each patient: on Days 0 (right after the implant), 7, and 30. Axial CT images were taken with the patient in the supine position on a Lightspeed Plus CT Scanner (General Electric Medical Systems, Waukesha, WI). The slices were obtained at 1.25-mm intervals without an interslice gap. A 14F Foley urinary catheter was inserted for urethral localization on Day 30 but not on Day 7. Immediately after the CT scan, axial MRI (1.5 T Sigma, General Electric Medical Systems) was obtained using T_2-weighted sequences with a pelvic coil. The slice thickness was 3 mm, with no interslice gap. CT-MRI fusion was performed manually by the brachytherapy dosimetrist (C.C. or A.L.), relying on the brachytherapy seeds as fiducial markers. Seed location was determined by VariSeed on the CT images, and the seed count was verified manually using orthogonal pelvic X-rays. All relevant soft-tissue structures were contoured on the MRI scans. Pre- and postimplant contouring was performed and/or reviewed by the same experienced physician (J.C.).

Orthogonal X-rays of the pelvis (anteroposterior and oblique) and chest (anteroposterior and lateral) were taken at 1 month to count the seeds and evaluate any seed migration or loss. The sequential CT scans were helpful to assess seed displacement within the pelvis. All patients were asked to strain their urine for 3 days, to use condoms for the initial three to four sexual encounters, and to return any seeds lost in urine or ejaculate in the lead pouch provided.

The prostate edema factor was calculated as the percentage difference in prostate volume as measured on MRI at each point (Days 0, 7, and 30) compared with the preimplant prostate volume calculated by TRUS planimetry. The edema factor at each point was compared between the two cohorts. Implant quality was assessed using V_{100} and V_{150} and D_{90}. A comparison of the prostate V_{100} between the LS and SS cohorts was performed using absolute values, because the preimplant values were identical. For the prostate V_{150} and D_{90}, the baseline values were slightly different; hence, comparisons were done, not only with absolute values, but also with the percentage difference from the baseline values. Critical organ dosimetry (rectal wall and urethra) and the acute toxicity profile have been reported separately (25).

Statistical analysis

Descriptive statistics were used for the baseline characteristics of both cohorts. Prostate volume, edema factor, and dosimetry (both absolute values and the percentage difference from baseline) at each point were compared using a two-sided unpaired Student's *t* test. Only descriptive statistics were used for seed loss and migration for both cohorts.

RESULTS

The pretreatment characteristics were similar in the two cohorts (Table 1). The mean baseline prostate volume was

Table 2. Dosimetric comparison of loose seeds and strands

Parameters	Loose seeds Mean ± SD	Edema %	Strands Mean ± SD	Edema %	*p* value (*t* test)
Pre implant vol	34.5 ± 10.8		40.8 ± 13		0.1
volume day 0	45.1 ± 12.1	33.9 ± 19	53.5 ± 17	31 ± 13	0.09
volume day 7	42.1 ± 12.6	23.3 ± 13	49.2 ± 15	20.4 ± 12	0.1
volume day 30	36.9 ± 11.5	7.2 ± 15	41.1 ± 12	2.4 ± 11	0.3
V100 % pre	100		100		
day 0	93.2 ± 3.8		89.2 ± 4.5		0.004
day 7	93.1 ± 4.6		92.8 ± 2.7		0.8
day 30	94.9 ± 4.0		95.6 ± 3.2		0.5
D90Gy pre	179.2 ± 7		178.4 ± 5		0.7
day 0	153.9 ± 11	14.1 ± 5.3	144.2 ± 8	19.1 ± 5	0.003
day 7	155.7 ± 13.5	12.6 ± 7	152.5 ± 9	14.0 ± 5	0.4
day 30	163.7 ± 16.9	7.7 ± 12.3	166.9 ± 14	14.0 ± 5	0.3
V150 % pre	60.7 ± 0.4		58.2 ± 3.3		0.02
day 0	44.8 ± 7.8	25.4 ± 11	38.6 ± 6.6	33.8 ± 10	0.01
day 7	49.2 ± 8.6	19 ± 13	46.0 ± 7.0	20.7 ± 12	0.2
day 30	60.4 ± 10.4	0.7 ± 15.7	58.3 ± 9.7	−0.6 ± 18	0.5

Abbreviations: SD = standard deviation, pre = pre implant, V100, VI50 = % of prostate volume enclosed by 100% and 150% isodose.

slightly greater in the SS cohort compared with the LS cohort (40.8 ± 13.3 cm^3 vs. 34.5 ± 10.8 cm^3, $p = 0.1$). The edema factor at all time points was greater for LSs than for SSs but did not reach statistical significance (Table 2). In both cohorts, the dosimetric quality parameters showed the largest deterioration from the preplan values immediately after implantation and then improved to the preplan values or greater as the edema resolved.

Dosimetry

The mean V_{100} on Day 0 was greater with LSs than with SS (93.2% ± 3.8% vs. 89.2% ± 4.5%, $p = 0.004$). Similarly, the mean D_{90} on Day 0 was greater with LSs than with SS (153.9 Gy ± 10.8 vs. 144.2 Gy ± 7.9, $p = 0.003$). Also, the LS cohort had less of a decrease in D_{90} on Day 0 (14% vs. 19%, $p = 0.004$) compared with the SS cohort. The preplan V_{150} was lower in the SS cohort than in the LS cohort (58.2% ± 3.3% vs. 60.7% ± 3.4%), which could have contributed to the lower V_{150} values with SSs on Day 0 (38.6% ± 6.6% vs. 44.8% ± 7.8%). However, the SS cohort also had a greater percentage decrease in V_{150} on Day 0 compared with the preplan (33.8% ± 9.7% vs. 25.4% ± 10.8%). On Days 7 and 30, the absolute values, as well as the percentage difference from the preplan for all dosimetric variables (V_{100}, V_{150}, and D_{90}) were similar for both cohorts (Table 2).

Seed migration and loss

Seed migration to the lung, as assessed at 1 month by posteroanterior and lateral chest X-rays, was observed in 4 patients (total five seeds) in the LS cohort. Seed migration did not occur in the SS cohort. One patient in the LS cohort lost 6 seeds through ejaculation during the second week after implantation. In the SS cohort, 5 patients reported seed loss (total 22 seeds; 8 seeds for 1 patient, 5 seeds for 1 patient, and 3 seeds each by 3 other patients). Overall, 13 seeds were lost in 5 patients in the LS cohort (0.6% of total) and 24 seeds were lost for 6 patients in the SS cohort (1.1% of total; Table 3).

The finding of increased seed loss through the urinary tract in the SS cohort was unexpected. Strand movement in the Z-axis direction (Fig. 1) was observed on the sequential scans. In the patients who lost seeds through the urinary tract, each strand was identified on the sequential scans and color coded. It was evident that some strands moved superiorly (cranially, Z-axis) from their position on Day 0 and into the bladder as seen on Day 7 and were absent on Day 30 scans. Additional analysis is underway to evaluate the relative seed positions and movement over time for both cohorts.

DISCUSSION

Seed migration to the lung through the pelvic veins after permanent prostate implantation using loose ^{125}I or ^{103}Pd seeds is a matter of concern for both patients and physicians (1–5). Recent reports of rare events such as seed migration to the coronary arteries or the heart (6, 7) highlight the importance of avoiding seed loss in the periprostatic veins. Seed migration to the lungs has been reported to occur in 5.9–55% of patients (Table 4). Chest X-ray is the standard tool used to evaluate seed loss to the lungs, but the timing of assessment has been variable, as has been the number of views taken (posteroanterior only vs. posteroanterior and lateral).

Table 3. Comparison of seed loss

Seed loss site	LSs (*n*)	SSs (*n*)
Bladder	1	1
Urine	1	22 (5 patients)
Pelvis	0	1
Lung	5 (4 patients)	0
Ejaculate	6 (1 patient)	0
Total seeds (%)	13/2,160 (0.6)	24/2,236 (1.1)
Total patients (*n*)	5/20	6/20

Abbreviations as in Table 1.

This variability might have contributed to the range of reported seed loss, as would technical factors such as the total number of seeds implanted, the percentage of seeds implanted outside the prostate, and the use of SSs. The percentage of seeds migrating to lung has ranged from 0.1% to 0.9% of the total number implanted (Table 4). Stranding of seeds has been shown to essentially eliminate seed migration to the lungs (8–10), and the results of the present study have confirmed this. The 20% of patients in the LS cohort experiencing seed loss to the lungs was also consistent with the rates reported in previous studies (2–5, 9–11) (Table 4).

Merrick *et al.* (11) documented total seed loss over time after brachytherapy using chest and pelvic X-rays. The proportion of patients experiencing seed loss from the prostate region increased from 76% at 1 month to 93% at 6 months for LSs and from 60% to 80%, respectively, for SSs. The investigators reported a similar rate of seed migration to the lungs for LSs (22.2%) and for SSs (21.4%). However, their SS technique generally used a mixture of LSs and SSs, with about one third being LSs. Another important observation by Merrick *et al.* (11) was that seed migration to the lungs accounted for only 10% of total seed loss from the prostate region, highlighting the importance of other mechanisms of loss.

Fuller *et al.* (10) compared seed loss between LSs and SSs using serial X-rays of the pelvis (anterior and lateral) and chest (posteroanterior only) starting from Day 1 after implant

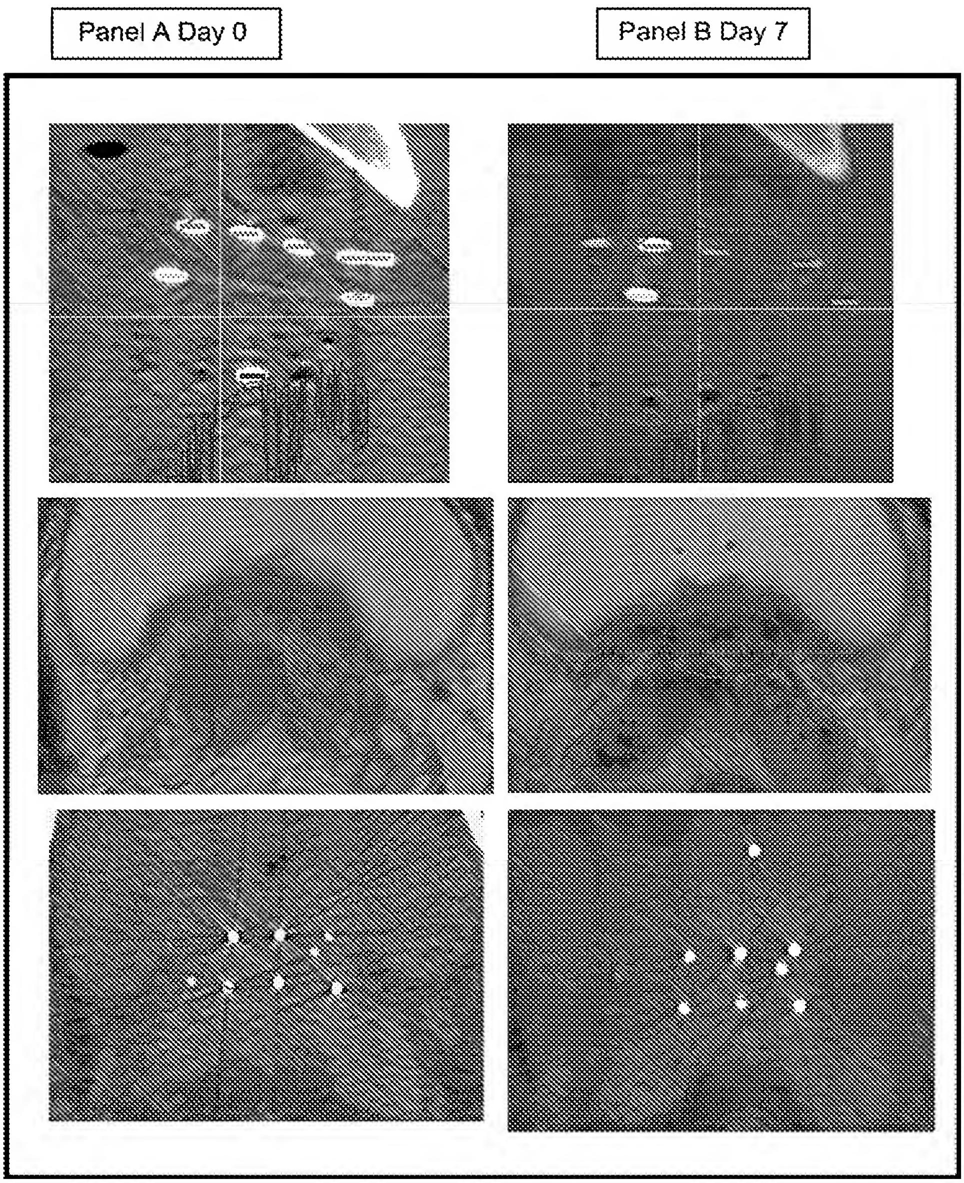

Fig. 1. (Panel A) Images from Day 0 scans. (Panel B) Images from Day 7 scans. (Top) Two-dimensional reconstruction from computed tomography scan showing specially loaded five-seed strand (double-loaded at apical end; all seeds stranded). Between Days 0 and 7, cranial movement of strand into bladder seen. This was one of two strands that migrated cranially in this patient. (Middle) Magnetic resonance imaging scan slice near prostate base. Strands seen in bladder on Day 7. (Lower) Computed tomography images at same level as magnetic resonance images.

Table 4. Literature survey of seed migration to lung

Author (Ref.)	Number of patients	% with seed migration to lung	% of total seeds	Time of CXR
Eshleman *et al.* (5)	102	55 %	0.9	2-3 mo
Grima *et al.* (29)	221	17.6 %	–	day 1
Nag *et al.* (3)	107	17.8 %	0.3	1 mon
Older *et al.* (4)	110	29 %	–	day 1
Merrick *et al.* (11)	175	21.8 % (SS 21% ; LS 22%)	0.25	day 1 to >1 yr
Tapen *et al* (9)	289	5.9% (SS 0.7%; LS 11%)	–	day 1. PA only
Fuller *et al.* (10)	60	15% (SS 0%; LS 24%)	0.1	day 1-1 yr. PA only
Present study	40	10 % (SS 0 %; LS 20%)	0.1	day 30

Abbreviations: SS =strands; LS = loose seeds; CXR = Chest X-ray; PA = postero-anterior.

to ≤1 year after permanent implantation. Seed movement within the pelvis was found to be either to the seminal vesicles proximal to the prostate, distal to the prostate, or laterally within the pelvis. The use of SSs reduced overall seed loss (35% vs. 62%), with seed migration to the lungs being 0% vs. 24% and distal migration within the pelvis being 9% vs. 35%. That study defined seed migration to the seminal vesicles or distal to the prostate as displacement of >1 cm beyond the "main seed cluster."

Reed *et al.* (17) reported a randomized comparison of LSs versus SSs and documented that seed loss occurred in 47% of patients (15 of 32) implanted with LSs vs. 23% (6 of 30) when SSs were used. Chest X-rays were not routinely performed and mechanisms of seed loss were not reported. Of the SS patients, 10% lost multiple seeds, and the investigators noted a trend to a lower V_{100} and D_{90} in the SS cohort.

In the present study, 25% (5 of 20) of the LS cohort lost seeds compared with 30% (6 of 20) of the SS cohort. We documented seed loss in the urine, in ejaculate, and within the pelvis; however, we did not evaluate distal migration or migration proximally into the seminal vesicles. Furthermore, our evaluation was limited to the initial month after the implantation. A summary of the studies evaluating seed loss is given in Table 5.

None of the above-mentioned studies (10, 11, 17) evaluated seed loss through the urinary tract specifically. From a previous era, Sommerkamp *et al.* (20) observed that 90% of men implanted with loose ^{125}I seeds using an open retropubic manually guided implantation technique lost seeds during a 62-month period. Most of the seeds were lost through the urinary tract. However, the technique of implantation in the early 1980s was not comparable to that of modern image-guided brachytherapy. Without visualization of either the urethra or prostate–bladder interface, a high rate of seed loss is to be expected. More recently, Stutz *et al.* (19) reviewed the physics log book for more than 1,700 patients who had undergone implantation during a 5-year period from 1997 to 2002 and reported that 30% had lost seeds through the urinary tract. However, in that study, the early cohort was implanted without the benefit of sagittal TRUS imaging to identify the bladder–prostate interface. Furthermore, urethral contrast was not used intraoperatively for any of the patients, even those who had previously undergone transurethral resection of the prostate. Both of these technical factors could have contributed to a greater rate of seed loss. Despite a preference for SSs for ^{125}I in the study by Stutz *et al.* (19), a greater incidence of seed loss was seen for the ^{125}I cohort than for the LS ^{103}Pd cohort (0.61% vs. 0.45%, p = 0.009). The investigators speculated that this might have been resulted from withdrawal of protruding strands from the bladder at cystoscopy.

In our study, 5 of 20 patients in the SS cohort reported seed loss through the urine and 3 returned strands or partial strands at the 1-month assessment. Overall, 22 seeds were lost (Table 3), and only 1 seed was lost in the urine in the LS cohort. This major route of loss through the urinary tract for SSs was quite unexpected. Fluoroscopic images taken intraoperatively demonstrated apparently good strand position (Fig. 2), as did the Day 0 scans (MRI and CT). Although our implantation technique clearly worked well for LSs (one seed only lost in urine in 20 patients), it might not be ideal for SSs. If at needle insertion, the needle tip transgresses the bladder wall and then is brought back so that the tip is just within the prostatic base, it might have created a tract through which a stiff strand can be extruded during muscular effort to void. In our experience, this technique has led to excellent

Table 5. Comparison of seed loss in published studies

Investigator/patients (n)	Patients with seed loss at specified point: LSs	Patients with seed loss at specified point: SSs
Merrick *et al.* (11)/175	76% at 1 mo; 93% at 6 mo	60% at 1 mo; 80% at 6 mo
Reed *et al.* (17)/64	47% at 1 mo	23% at 1 mo
Fuller *et al.* (10)/60	62% at 1 y; lung 24%, distal 35%, SVs 32%, lymphatics 5%	35% at 1 y; SVs 30%, distal 9%
Present study/40	25% at 1 mo; lung 20%, ejaculate 5%, bladder 5%, urine 5%	30% at 1 mo; pelvis 5%, bladder 5%, urine 25%

Abbreviations: SVs = seminal vesicles; other abbreviations as in Table 1.

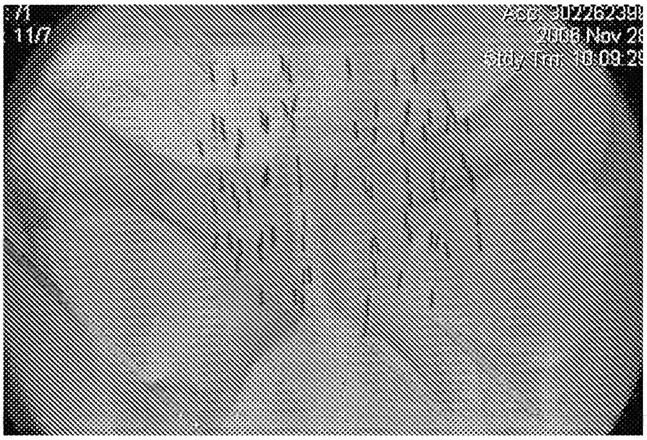

Fig. 2. Fluoroscopic image at completion of implant shown in Fig. 1.

coverage of the base when using LSs; however, it should perhaps be modified when using SSs.

Our study was designed to sequentially evaluate SSs in terms of seed stability, edema resolution, and prostate dosimetry and to compare these findings with those from a similar cohort treated with LSs. Unlike many other reports, only SSs were used in our SS cohort, without the addition of any LSs (10–12, 14, 17). Prostate edema at all points was slightly less with SSs compared with LSs, but the difference did not reach statistical significance. All the prostate dosimetry factors (V_{100}, V_{150}, and D_{90}) were significantly better with LSs on Day 0. This difference was no longer seen on Days 7 and 30 and thus is probably of no significance clinically.

The use of CT-MRI fusion for postimplant dosimetry offers an unparalleled advantage over CT for prostate definition (25), and the use of sequential evaluations allows for the tracking of changes in dosimetry during the first month after implantation. Although these two cohorts were not randomized, the pretreatment characteristics were similar and a consistent planning approach was used. No identifiable modifications in technique were made in the interval between treating the two cohorts, and all implantations were performed by a single experienced physician.

The studies comparing prostate dosimetry between SSs and LSs are summarized in Table 6. Studies by Lee *et al.* (12) and Fagundes *et al.* (14) documented better V_{100} and D_{90} on CT postimplant dosimetry for SSs compared with that for LSs. Both of these studies might have been influenced by the "learning curve" effect, because LSs were used in the beginning of the institutional practice with later adoption of a SS product. Heysek *et al.* (16) found that although the V_{100} was similar, the D_{90} was better with SSs at Day 30. In contrast, Fuller *et al.* (10) found no dosimetric differences in terms of V_{100}, V_{150}, and D_{90} for SSs vs. LSs. All these retrospective studies performed postimplant dosimetry at one point only (either Day 0 or Day 30) using CT only. The randomized study by Reed *et al.* (17) ($n = 62$) had the advantage of using CT-MRI fusion to evaluate the postimplant dosimetry and also evaluated it at two points (Days 0 and 30).

Table 6. Literature survey of comparison of dosimetry between loose seeds and stranded seeds

		V100 (%)		D90 (Gy)		V150 (%)	
Author (Ref.)	No. of patients	day 0	day 30	day 0	day 30	day 0	day 30
Lee *et al.* (12)	40						
Strands		–	94.1	–	164.2	–	–
Loose			86.5		132.1		
p value			< 0.001		< 0.001		
Fagundes *et al.* (14)	473						
Strands		92.5	–	157.8	–	46.5	–
Loose		89.3		149.9		59.8	
p value		< 0.05		< 0.05		< 0.05	
Fuller *et al.* (10)	60						
Strands		97.3	–	164.4	–	57.5	–
Loose		95.7		158.3		54.6	
p value		ns		ns		ns	
Heysek *et al.* (16)	272						
Strands		–	89.1	–	147.8	–	–
Loose			88.7		144		
p value			ns		0.04		
Reed *et al.* (17)	64						
Strands		95	94	169	164	–	–
Loose		95	96	169	178		
p value		ns	ns	ns	0.05		
Present study							
Strands		89.2	95.6	144	167	39	58
Loose		93.2	94.9	154	164	45	60
p value		0.004	ns	0.003	ns	0.01	ns

Abbreviations: V100, V150 = % of prostate volume enclosed by 100% and 150% isodose; D90 = Minimum dose in Gray received by 90% of prostate volume; ns = non significant.

They did not observe any dosimetric advantage with SSs and, in fact, demonstrated a greater D_{90} on Day 30 with LSs.

We observed some movement of entire strands in the craniocaudal direction (Z-axis), which might have been a result of the effect of contractions of the pelvic musculature. Relatively stiff strands do not kink or offer resistance to craniocaudal displacement. Sequential scans of the patient who lost eight seeds (two strands) in urine revealed cranial movement of the strands into the bladder on Day 7 compared with Day 0 and the subsequent absence of the two strands on the Day 30 scans (Fig. 1). We also observed significant caudal movement in some patients, similar to the increased Z-axis movement observed by McLaughlin *et al.* (23) on CT-MRI fusion performed on Days 0 and 14. They reported a paradoxical change in D_{90} (absence of improvement in D_{90} despite prostate edema resolution) with SSs over time, along with a significant increase in the dose to the rectal wall and external sphincter because of migration of SSs in the caudal direction.

Pinkawa *et al.* (26) evaluated the movement of seeds at the prostate base and apex, (representing the lead and final seeds of five strands) in 51 patients on Days 0 and 30 using CT. The displacement was correlated with the isodose contours relative to the pelvic bony structures without consideration of the prostate contour. They documented significant isodose displacement inferiorly and posteriorly, presumably owing to resolution of prostate and periprostatic edema. They noted greater displacement of SSs vs. single seeds and speculated that longer strands move more readily along a previous needle track. Single seeds or short strands are more likely to tilt within prostatic tissue and, because they do not remain aligned with their entry track, are less susceptible to movement. The observed increase in rectal dose between Days 0 and 30 secondary to edema resolution has been previously documented (27).

The effect of seed displacement and loss on the dosimetry of the prostate, as well as of critical organs (rectum, urethra, and erectile tissue), might be more pronounced with SSs than with LSs, because this involves movement and/or loss of multiple seeds. An extensive analysis of individual seed positions and strand movement on sequential scans for both cohorts is underway and may elucidate our findings. One limitation of our study was that the implants were performed by a single experienced practitioner (J.C.). Contouring was performed by either the brachytherapy fellow (E.P.S.) or one of the brachytherapy dosimetry staff (C.C. or A.L.) and reviewed by the practitioner (J.C.). However, all final contours and postplan dosimetry were reviewed in the weekly quality assurance rounds by the entire team, including two physicists (J.B., I.Y.) and another radiation oncologist.

CONCLUSIONS

The results of our study have highlighted that strand displacement and loss can occur despite the elimination of seed loss through the pelvic veins to the lung. The overall seed loss was surprisingly greater in the SS cohort than in the LS cohort, with most occurring through the urinary tract. Awareness of this mechanism of loss could allow for subtle modifications of technique to avoid the possibility of overinsertion of a needle at the base of the prostate and creation of a track for subsequent strand extrusion. In our study, the prostate dosimetry was similar at Days 7 and 30 for the two cohorts. SSs continue to have a distinct advantage over LSs in the elimination of venous seed migration.

REFERENCES

1. Steinfeld AD, Donahue BR, Plaine L. Pulmonary embolization of iodine-125 seeds following prostate implantation. *Urology* 1991;37:149–150.
2. Grimm PD, Blasko J, Ragde H, *et al.* Migration of iodine-125 and palladium-103 seeds to the lung after transperineal brachytherapy for prostate cancer. *Endocurie/Hypertherm Oncol* 2000; 9:50.
3. Nag S, Vivekanandam S, Martinez-Monge R. Pulmonary embolization of permanently implanted radioactive palladium-103 seeds for carcinoma of the prostate. *Int J Radiat Oncol Biol Phys* 1997;39:667–670.
4. Older RA, Synder B, Krupski TL, *et al.* Radioactive implant migration in patients treated for localized prostate cancer with interstitial brachytherapy. *J Urol* 2001;165:1590–1592.
5. Eshleman JS, Davis BJ, Pisansky TM, *et al.* Radioactive seed migration to the chest after transperineal interstitial prostate brachytherapy: Extraprostatic seed placement correlates with migration. *Int J Radiat Oncol Biol Phys* 2004; 59:419–425.
6. Davis BJ, Pfeifer EA, Wilson TM, *et al.* Prostate brachytherapy seed migration to the right ventricle found at autopsy following acute cardiac dysrhythmia. *J Urol* 2000;164:1661.
7. Davis BJ, Bresnahan JF, Stafford SL, *et al.* Prostate brachytherapy seed migration to a coronary artery found during angiography. *J Urol* 2002;168:1103.
8. Kumar PP, Good RR. Vicryl carrier for I-125 seeds: Percutaneous transperineal insertion. *Radiology* 1986;159:276.
9. Tapen EM, Blasko JC, Grimm PD, *et al.* Reduction of radioactive seed embolization to the lung following prostate brachytherapy. *Int J Radiat Oncol Biol Phys* 1998;42:1063–1067.
10. Fuller DB, Koziol JA, Feng AC. Prostate brachytherapy seed migration and dosimetry: Analysis of stranded sources and other potential predictive factors. *Brachytherapy* 2004;3:10–19.
11. Merrick GS, Butler WM, Dorsey AT, *et al.* Seed fixity in the prostate/peri-prostatic region following brachytherapy. *Int J Radiat Oncol Biol Phys* 1998;46:215–220.
12. Lee WR, deGuzman AF, Tomlinson SK, *et al.* Radioactive sources embedded in suture are associated with improved postimplant dosimetry in men treated with prostate brachytherapy. *Radiother Oncol* 2002;65:123–127.
13. Crook J, PS, Williams T, *et al.* The pros and cons of linked vs. loose seeds. *Radiother Oncol* 2003;69:63–72.
14. Fagundes HM, Keys RJ, Wojcik MF, *et al.* Transperineal TRUS-guided prostate brachytherapy using loose seeds versus RAPIDStrand: A dosimetric analysis. *Brachytherapy* 2004;3: 136–140.
15. Kaplan ID, Meskell PM, Lieberfarb M, *et al.* A comparison of the precision of seeds deposited as loose seeds versus suture embedded seeds: A randomized trial. *Brachytherapy* 2004;3:7–9.

16. Heysek RV, Gwede CK, Torres-Roca J, *et al.* A dosimetric analysis of unstranded seeds versus customized stranded seeds in transperineal interstitial permanent prostate seed brachytherapy. *Brachytherapy* 2006;5:244–250.
17. Reed DR, Wallner KE, Merrick GS, *et al.* A prospective randomized comparison of stranded vs. loose 125I seeds for prostate brachytherapy. *Brachytherapy* 2007;6:129–134.
18. Coakley FV, Hricak H, Wefer AE, *et al.* Brachytherapy for prostate cancer: Endorectal MR imaging of local treatment-related changes. *Radiology* 2001;219:817–821.
19. Stutz M, Petrikas J, Raslowsky M, *et al.* Seed loss through the urinary tract after prostate brachytherapy: Examining the role of cystoscopy and urine straining post implant. *Med Phys* 2003;30: 2695–2698.
20. Sommerkamp H, Rupprecht M, Wannenmacher M. Seed loss in interstitial radiotherapy of prostatic carcinoma with I-125. *Int J Radiat Oncol Biol Phys* 1988;14:389–392.
21. Waterman FM, Dicker AP. Impact of postimplant edema on V(100) and D(90) in prostate brachytherapy: Can implant quality be predicted on day 0? *Int J Radiat Oncol Biol Phys* 2002;53: 610–621.
22. Taussky D, Austen L, Toi A, *et al.* Sequential evaluation of prostate edema after permanent seed prostate brachytherapy using CT-MRI fusion. *Int J Radiat Oncol Biol Phys* 2005;62: 974–980.
23. McLaughlin PW, Narayana V, Drake DG, *et al.* Comparison of MRI pulse sequences in defining prostate volume after permanent implantation. *Int J Radiat Oncol Biol Phys* 2002;54: 703–711.
24. Crook J, Milosevic M, Catton P, *et al.* Interobserver variation in postimplant computed tomography contouring affects quality assessment of prostate brachytherapy. *Brachytherapy* 2002;1: 66–73.
25. Saibishkumar EP, Borg J, Yeung I, *et al.* Loose seeds versus stranded seeds: A comparison of critical organ dosimetry and acute toxicity in iodine 125 permanent implant for low risk prostate cancer. *Brachytherapy* 2008;7:200–205.
26. Pinkawa M, Asadpour B, Gagel B, *et al.* Evaluation of source displacement and dose–volume changes after permanent prostate brachytherapy with stranded seeds. *Radiother Oncol* 2007;84:190–196.
27. Taussky D, Yeung I, Williams T, *et al.* Rectal-wall dose dependence on postplan timing after permanent-seed prostate brachytherapy. *Int J Radiat Oncol Biol Phys* 2006;65:358–363.